

Appln. No. 09/889,936  
Amd. dated April 3, 2006  
Reply to Office Action of October 6, 2005

**Amendments to the Claims**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

Claims 1-78 (Cancelled).

79 (Currently amended). ~~A protein~~ An antibody or antibody fragment, comprising heavy and light chain variable region sequences of SEQ ID NOS: 6 and 8 ~~an antigen-binding portion formed by two cooperating peptide sequences of Fig. 3A and Fig. 3B or comprising an altered antigen-binding portion where at least one of peptide sequences an altered sequence, being a sequence of one or both of Fig. 3A and 3B in which one or more of an amino acid residue has been added, deleted or replaced by another amino acid residue, with the altered antigen-binding portion retaining substantially the same antigen-binding specificity as said antigen-binding portion.~~

80 (Currently amended). ~~A protein according to The antibody or antibody fragment of Claim 79~~ selected from the group consisting of monoclonal antibodies, IgM antibodies, IgG antibodies, a fragment of an antibody comprising an antigen-binding domain, an antibody without the Fc region, and a single chain antibody, a fragment of any of the above retaining substantially the same antigen-binding specificity as said antigen-binding portion.

81 (Currently amended). ~~A protein according to The antibody or antibody fragment of Claim 80, being which is a~~

monoclonal antibody designated herein as the 5B3 monoclonal antibody.

Claim 82 (Cancelled) .

83(Withdrawn and Currently Amended) . Apparatus for detecting small assayed molecules in a sample, comprising:

(a) a sensing member comprising a piezoelectric crystal having at least one sensing surface which can interact with a medium in contact therewith by either binding a first indicator agent from the medium, or by releasing a second indicator agent originally immobilized on the sensing surface into the medium;

the medium being either the sample, in which case the assayed molecule present[[,] causes the release of the second indicator agent from the at least one sensing surface, or ~~being~~ a treated sample preparation obtained by reacting the sample with one or both of a reagent solution or sample-processing hardware, such that said medium comprises a first indicator agent or a second indicator agent-releasing species at a concentration of said agent or species which is in correlation to the concentration of the assayed molecule in the sample, the binding or release resulting in a change of mass of the sensing surface[;],

wherein:

said at least one sensing surface carries capturing agents which bind to neutralizing agents at an assayed molecule-binding domain of the neutralizing agent[,,];

~~and wherein~~ said capturing agents are assayed molecules, residues or moieties and said neutralizing

agents comprise first antibodies which bind to the assayed molecules[, ,]; and

~~and wherein~~ said first antibodies are a plurality of  
an antibody or antibody fragment that comprises heavy and  
light chain variable region sequences of SEQ ID NOS:6 and  
8 have the binding characteristics of the 5B3 monoclonal  
antibody;

- (b) a testing cell for holding said medium and bringing it into contact with said at least one sensing surface; and
- (c) an electric or electronic utility for inducing vibrations in the piezoelectric crystal and measuring resonance frequency thereof, a change in resonance frequency after contact between the sensing surface and the medium, indicating presence of the assayed molecules in the sample.

84 (Withdrawn). An apparatus according to Claim 83, wherein the degree of change in resonance frequency serves as a measure of the level of said assayed molecule in said sample.

85 (Withdrawn). An apparatus according to Claim 83, wherein said assayed molecule is an explosive molecule.

86 (Withdrawn and Currently Amended). An apparatus according to Claim 83, wherein said first ~~antibody~~ is the antibodies are 5B3 monoclonal antibody antibodies.

87 (Withdrawn and Currently Amended). An apparatus according to Claim 83, wherein said at least one sensing surface carries residues or moieties of the assayed molecules bound to said first antibodies which can competitively bind to

soluble assayed molecules in a medium in contact with the at least one sensing surface, whereby in the presence of the assayed molecules in said medium the first antibodies are released from the at least one sensing surface.

88(Withdrawn). An apparatus according to Claim 87, wherein the first antibodies are bound or complexed to a mass-increasing agent.

89(Withdrawn). An apparatus according to Claim 88, wherein said mass increasing agent comprises a second antibody which binds to said first antibody, or comprises avidin or streptavidin bound to a biotin residue conjugated to the first antibody.

90(Withdrawn). An apparatus according to Claims 83, wherein said assayed molecule is DNT or TNT.

91(Withdrawn). A system for detecting small assayed molecules in a sample comprising an apparatus according to Claim 83 and one or both of reagents and hardware for processing said sample or for introducing it into said cell.

92(Withdrawn). A system according to Claim 91, wherein said hardware comprises a flow system for propelling a medium comprising the sample into said cell.

93(Withdrawn and Currently Amended). A system according to Claim 91, comprising:

- (a) a sensing member comprising a piezoelectric crystal having at least one sensing surface which carries

residues or moieties of said assayed molecules bound to a first antibody or antibody fragment that comprises heavy and light chain variable region sequences of SEQ ID NOS:6 and 8 ~~protein molecule which has the binding characteristics of the 5B3 monoclonal antibody;~~

- (b) a testing cell for holding a medium and bringing it into contact with said at least one sensing surface, whereby in the ~~present presence~~ of the assayed molecules in the medium, at least some of ~~said protein molecules~~ a plurality of said first antibody or antibody fragment are released into the medium;
- (c) hardware for introducing the sample into the testing vessel; and
- (d) an electric or electronic utility for inducing vibrations in the piezoelectric crystal and measuring resonance frequency thereof, a reduction in resonance frequency after contact between the sensing surface and the medium, indicating presence of said assayed molecule in the sample.

94 (Withdrawn). A system according to Claim 93, wherein said assayed molecule is an explosive molecule.

95 (Withdrawn). A system according to Claim 94, wherein the assayed molecule is DNT or TNT.

96 (Withdrawn and Currently Amended). A system according to Claim 93, wherein ~~the protein molecules are said first antibody or antibody fragment is bound to a mass-increasing agents agent.~~

97 (Withdrawn and Currently Amended). A system according to Claim 96, wherein said mass increasing agent comprises a second antibody, or avidin or a streptavidin which bind to a biotin moiety conjugated to ~~the protein molecule~~ said first antibody or antibody fragment.

98 (Withdrawn and Currently Amended). A system according to Claim 91, comprising:

- (a) a sensing member comprising a piezoelectric crystal having at least one sensing surface which carries residues or moieties of the assayed molecules;
- (b) a reagent system comprising a first antibody or antibody fragment that comprises heavy and light chain variable region sequences of SEQ ID NOS:6 and 8 a protein molecule which has the binding characteristics of the 5B3 monoclonal antibody;
- (c) a testing cell for holding a medium and bringing it into contact with said at least one sensing surface, whereby in the presence of the assayed molecules in the medium, at least some of a plurality of said monoclonal antibodies first antibody or antibody fragment are released into the medium;
- (d) an arrangement for contacting the sample with said reagent system to obtain a treated sample preparation and for introducing the treated sample preparation into the testing vessel; and
- (e) an electric or electronic utility for inducing vibrations in the piezoelectric crystal and measuring resonance frequency thereof, a decrease in resonance frequency after contact between the sensing surface and the treated

sample preparation, indicating that the sample is free of the assayed molecules.

99(Withdrawn). A system according to Claim 98, wherein the assayed molecule is an explosive molecule.

100(Withdrawn). A system according to Claim 99, wherein the assayed molecule is DNT or TNT.

101(Withdrawn and Currently Amended). A system according to Claim 98, comprising a mass-increasing agent for binding to said first antibody or antibody fragment protein molecule.

102(Withdrawn and Currently Amended). A system according to Claim 101, wherein said mass increasing agent comprises a second antibody, or avidin or streptavidin which bind to a biotin moiety conjugated to said first antibody or antibody fragment the protein molecule.

103(Withdrawn and Currently Amended). A system according to Claim 91, comprising:

- (a) a sensing member comprising a piezoelectric crystal having at least one sensing surface which carries capturing agents for binding to an antibody or antibody fragment that comprises heavy and light chain variable region sequences of SEQ ID NOS:6 and 8a protein molecule which has the binding characteristics of the 5B3 monoclonal antibody;
- (b) a testing cell for holding a medium and bringing it into contact with said at least one sensing surface;

- (c) a reagent system comprising said ~~protein-molecule~~ antibody or antibody fragment which can bind to the assayed molecules;
- (d) an arrangement for contacting the sample with the reagent system under condition and for a time permitting binding of said ~~protein-molecule~~ antibody or antibody fragment to the assayed molecules, to obtain a treated sample preparation;
- (e) a filtration system for filtering out from said treated sample preparation of said ~~protein-molecule~~ antibody or antibody fragment unbound to an explosive molecule to obtain a filtrate essentially devoid of such unbound ~~said protein-molecule~~ antibody or antibody fragment;
- (f) arrangement for transfer of said filtrate to said testing cell; and
- (g) an electric or electronic utility for inducing vibrations in the piezoelectric crystal and measuring resonance frequency thereof, an increase in resonance frequency after contact between the sensing surface and the filtrate, indicating presence of the assayed molecules in the sample.

104 (Withdrawn). A system according to Claim 103, wherein the assayed molecule is an explosion molecule.

105 (Withdrawn). A system according to Claim 104, wherein the assayed molecule is DNT or TNT.

106 (Withdrawn). A system according to Claim 103, wherein said filtration system comprises immobilized residues or moieties of molecules of the assayed molecule.

107 (Withdrawn and Currently Amended). A system according to Claim 103, wherein said ~~protein molecule antibody or antibody fragment~~ is conjugated to a moiety which binds to said capturing agents.

108 (Withdrawn). A system according to Claim 107, wherein said moiety is a biotin residue and said capturing agent is avidin or streptavidin.

109 (Withdrawn and Currently Amended). A system according to Claim 91, comprising:

- (a) a sensing member comprising a piezoelectric crystal having at least one sensing surface which carries capturing agents for binding to an antibody or antibody fragment that comprises heavy and light chain variable region sequences of SEQ ID NOS:6 and 8 a protein molecule which has the binding characteristics of the 5B3 monoclonal antibody;
- (b) a testing cell for holding a medium and bringing it into contact with said at least one sensing surface;
- (c) a reagent system comprising said ~~protein molecule antibody or antibody fragment~~ which can bind to the assayed molecules, said ~~protein molecule antibody or antibody fragment~~ being conjugated to an enzyme which can catalyze a reaction yielding an insoluble reaction product;
- (d) an arrangement for contacting the sample with the reagent system under conditions and for a time permitting binding of said ~~protein molecule antibody or antibody fragment~~

antibody fragment to the assayed molecules, to obtain a treated sample preparation;

- (e) a filtration system for filtering out from said treated sample preparation said ~~protein-molecule antibody or antibody fragment~~ unbound to an assayed molecule to obtain a filtrate essentially devoid of such unbound ~~protein-molecule antibody or antibody fragment~~;
- (f) arrangement for transfer of said filtrate to said testing cell;
- (g) an ensemble of reagents and conditions for inducing said enzyme to catalyze the reaction yielding the insoluble reaction product; and
- (h) an electric or electronic utility for inducing vibrations in the piezoelectric crystal and measuring resonance frequency thereof, an increase in resonance frequency after contact between the sensing surface and the filtrate or after permitting the enzyme to catalyze said reaction, indicating presence of the assayed molecule in the sample.

110 (Withdrawn). A system according to Claim 109, wherein the assayed molecule is an explosive molecule.

111 (Withdrawn). A system according to Claim 110, wherein the assayed molecule is DNT or TNT.

112 (Withdrawn). A system according to Claim 110, wherein said filtration system comprises immobilized residues or moieties of the assayed molecules.

113(Withdrawn). A system according to Claims 110, wherein said capturing agent is an immobilized antibody which binds a moiety of said enzyme, such binding not interfering with the catalytic activity of said enzyme.

114(Withdrawn). A system according to Claims 109, wherein said enzyme is selected from the group consisting of horseradish peroxidase, microperoxidase, alkaline phosphatasae, glucoseoxidase and galactosidase.

115(Withdrawn and Currently Amended). A method for detecting a small assayed molecule in a sample, comprising:

- (a) providing a sensing member comprising a piezoelectric crystal having at least one sensing surface which can interact with a medium in contact therewith by either binding a first indicator agent from the medium, or by releasing a second indicator agent originally immobilized on the sensing surface into the medium, said at least one sensing surface carries residues and moieties of the assayed molecule bound to a first antibody or antibody fragment that comprises heavy and light chain variable region sequences of SEQ ID NOS:6 and 8;
- (b) contacting the at least one sensing surface with a medium being either the sample in which case the assayed molecule if present causes the release of the second indicator agent from the sensing surface, or being a treated sample preparation obtained by reacting the sample with one or both of a reagent solution or sample-processing hardware, such that said medium comprises a first indicator agent or a second indicator agent-releasing species, at a concentration of said agent or

species which is in correlation to the concentration of the assayed molecule in the sample, the binding or release resulting in a change of mass of the sensing surface;

- (c) inducing vibrations in the piezoelectric crystal and measuring resonance frequency thereof; and
- (d) determining whether a change in resonance frequency after contact between the sensing surface and the medium occurred, such change indicating presence of the assayed molecule in the sample.

116(Withdrawn). A method according to Claim 115, wherein said small molecule is an explosive.

117(Withdrawn). A method according to Claim 116, wherein said explosive is DNT or TNT.

118(Withdrawn). A method according to Claim 115, wherein the degree of change in resonance frequency serves as a measure of the level of said molecule in said sample.

119(Withdrawn and Currently Amended). A method according to Claim 115, comprising:

- (a) providing a sensing member comprising a piezoelectric crystal having at least one sensing surface which carries residues or moieties of the assayed ~~molecules~~ molecule bound to a first antibody or antibody fragment that comprises heavy and light chain variable region sequences of SEQ ID NOS:6 and 8 ~~protein molecule which has the~~ ~~binding characteristics of the 5B3 monoclonal antibody;~~

- (b) contacting the sample with the at least one sensing surface;
- (c) inducing vibrations in the piezoelectric crystal and measuring resonance frequency thereof; and
- (d) determining whether there occurred an increase in resonance frequency after contact between the sensing surface and the medium, such increase indicating presence of the assayed molecule in the sample.

120 (Withdrawn). A method according to Claim 119, wherein the assayed molecules are explosive molecules.

121 (Withdrawn). A method according to Claim 120, wherein the assayed molecule is DNT or TNT.

122 (Withdrawn and Currently Amended). A method according to Claim 119, comprising binding a mass increasing agent to said first antibody or antibody fragment ~~the antibodies~~.

123 (Withdrawn and Currently Amended). A method according to Claim 122, wherein said mass increasing agent comprises a second antibody, or an avidin or a streptavidin molecule which binds to a biotin moiety conjugated to said first antibody or antibody fragment ~~the protein molecule~~.

124 (Withdrawn and Currently Amended). A method according to Claim 115, comprising:

- (a) providing a sensing member comprising a piezoelectric crystal having at least one sensing surface which carries residues or moieties of the assayed molecules;

- (b) contacting the sample with a protein molecule which has the binding characteristics of ~~the 5B3 monoclonal antibody said first antibody or antibody fragment~~ and incubating for a time allowing ~~the antibodies said first antibody or antibody fragment~~ to bind to the assayed molecules if present in the sample, to yield a treated sample preparation;
- (c) contacting the treated sample preparation with the at least one sensing surface;
- (d) inducing vibrations in the piezoelectric crystal and measuring resonance frequency thereof; and
- (e) determining whether there occurred a decrease in resonance frequency after contact between the sensing surface and the treated sample preparation, such decrease indicating presence of the assayed molecule in the sample.

125 (Withdrawn). A method according to Claim 124, wherein the assayed molecule is an explosive molecule.

126 (Withdrawn). A method according to Claim 125 wherein the assayed molecule is DNT or TNT.

127 (Withdrawn and Currently Amended). A method according to Claim 124, comprising binding a mass-increasing antibody to said first antibody or antibody fragment ~~the protein molecule~~.

128 (Withdrawn and Currently Amended). A method according to Claim 127, wherein said mass increasing agent comprises a second antibody, or an avidin or a streptavidin molecule which

binds to a biotin moiety conjugated to said first antibody or antibody fragment ~~the protein molecule~~.

129(Withdrawn and Currently Amended). A method according to Claim 115, comprising:

- (a) providing a sensing member comprising a piezoelectric crystal having at least one sensing surface which carries capturing agents for binding to a first antibody or antibody fragment that comprises heavy and light chain variable region sequences of SEQ ID NOS:6 and 8 ~~protein molecule which has the binding characteristics of the 5B3 monoclonal antibody~~;
- (b) contacting the sample with said ~~protein molecule~~ first antibody or antibody fragment which can bind to the assayed molecules under conditions and for a time permitting binding of said first antibody or antibody fragment ~~protein molecule~~ to the assayed molecules, to obtain a treated sample preparation;
- (c) filtering the treated sample preparation through filtration system to filter out said first antibody or antibody fragment ~~protein molecule~~ unbound to the assayed molecules to obtain a filtrate essentially devoid of such unbound first antibody or antibody fragment ~~protein molecule~~;
- (d) contacting said filtrate with the at least one sensing surface;
- (e) inducing vibrations in the piezoelectric crystal and measuring resonance frequency thereof; and
- (f) determining whether there occurred a increase in resonance frequency after contact between the sensing surface and the treated sample preparation, such increase

indicating presence of the assayed molecules in the sample.

130 (Withdrawn). A method according to Claim 129, wherein the assayed molecules are explosive molecules.

131 (Withdrawn). A method according to Claim 130, wherein the assayed molecule is DNT or TNT.

132 (Withdrawn). A method according to Claim 129, wherein said filtration system comprises immobilized residues or moieties of the assayed molecules.

133 (Withdrawn and Currently Amended). A method according to Claim 129, wherein said first antibody or antibody fragment ~~protein-molecule~~ is conjugated to a moiety which binds to said capturing agents.

134 (Withdrawn). A method according to Claim 133, wherein said moiety is a biotin residue and said capturing agent is avidin or streptavidin.

135 (Withdrawn and Currently Amended). A method according to Claim 115, comprising:

- (a) providing sensing member comprising a piezoelectric crystal having at least one sensing surface which carries capturing agents for binding to a first antibody or antibody fragment that comprises heavy and light chain variable region sequences of SEQ ID NOS:6 and 8 ~~protein molecule which has the binding characteristics of the 5B3 monoclonal antibody;~~

- (b) contacting the sample with said first antibody or antibody fragment protein molecule which can bind to the assayed molecules, said protein molecule being conjugated to an enzyme which can catalyze a reaction yielding an insoluble reaction product, for a time permitting binding of said first antibody or antibody fragment protein molecule to the assayed molecules, to obtain a treated sample preparation;
- (c) filtering the treated sample preparation through filtration system to filter out said first antibody or antibody fragment protein molecule unbound to the assayed molecules to obtain a filtrate essentially devoid of such unbound first antibody or antibody fragment protein molecule;
- (d) contacting said filtrate with the at least one sensing surface;
- (e) applying condition permitting the enzyme to catalyze the production of the insoluble reaction product;
- (f) inducing vibrations in the piezoelectric crystal and measuring resonance frequency thereof; and
- (g) determining whether there occurred a decrease in resonance frequency after contact between the sensing surface and said filtrate or after application of said conditions, such decrease indicating presence of the assayed molecules in the sample.

136(Withdrawn). A method according to Claim 135 wherein the assayed molecule is an explosive molecule.

137(Withdrawn). A method according to Claim 136, wherein the assayed molecule is DNT or TNT.

Appln. No. 09/889,936  
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138(Withdrawn). A method according to Claim 136, wherein said filtration system comprises immobilized residues or moieties of said assayed molecule.

139(Withdrawn). A method according to Claim 136, wherein said capturing agent is an immobilized antibody which binds a moiety of said enzyme, such binding not interfering with the catalytic activity of said enzyme.

140(Withdrawn). A method according to Claim 136, wherein said enzyme is selected from the group consisting of horseradish peroxidase, microperoxidase, alkaline phosphatase, glucoseoxidase and galactosidase.